WHAT IS CLAIMED:

1. A spot-on formulation for the treatment or prophylaxis of parasite infestation in mammals or birds which comprises

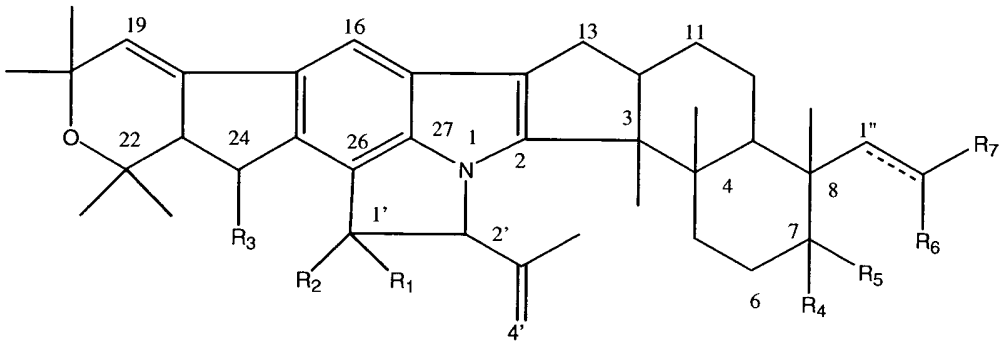
(1) an effective amount of at least one nodulisporic acid derivative

(2) a pharmaceutically or veterinary acceptable liquid carrier vehicle; and

(3) optionally, a crystallization inhibitor.

2. The spot-on formulation according to claim 1, which comprises:

(1) an effective amount of at least one nodulisporic acid derivative of the formula:



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wherein

R_1 is (1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted cycloalkyl,

(6) optionally substituted cycloalkenyl,

where the substituents on the alkyl, alkenyl, alkynyl, cycloalkyl and cycloalkenyl are 1 to 3 groups independently selected from

(i) alkyl,

(ii) X-alkyl, where X is O or $S(O)_m$,

(iii) cycloalkyl,

(iv) hydroxy,

(v) halogen,

(vi) cyano,

(vii) carboxy,

(viii) NY^1Y^2, where Y^1 and Y^2 are independently H or alkyl,

(ix) alkanoylamino, and

(x) aroylamino wherein said aroyl is optionally substituted with 1 to 3 groups independently selected from R^f

(7) aryl or arylalkyl wherein said aryl is optionally substituted with 1 to 3 groups independently selected from R^f,

(8) perfluoroalkyl

(9) a 5- or 6-member heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen atoms optionally substituted by 1 to 3 groups independently selected from hydroxy, oxo, alkyl and halogen, and which may be saturated or partly unsaturated,

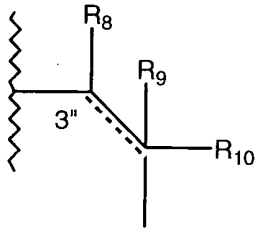
R_2, R_3, and R_4 are independently OR^a, OCO_2R^b, $OC(O)NR^cR^d$; or

R_1 and R_2 together represent =O, $=NOR^a$ or $=N\text{-}NR^cR^d$;

R_5 and R_6 are H; or

R_5 and R_6 together represent -O-;

R_7 is (1) CHO, or

(2) the fragment 

R_8 is (1) H,

(2) OR^a, or

(3) NR^cR^d

R_9 is (1) H, or

(2) OR^a;

R_{10} is (1) CN,

(2) $C(O)OR^b$,

(3) $C(O)N(OR^b)R^c$,

(4) $C(O)NR^cR^d$,

(5) $NHC(O)OR^b$,

(6) $NHC(O)NR^cR^d$,

(7) CH_2OR^a,

(8) $CH_2OCO_2R^b$,

(9) $CH_2OC(O)NR^cR^d$,

(10) $C(O)NRCNR^cR^d$, or

(11) $C(O)NR^cSO_2R^b$;

------ represents a single or a double bond;

R^a is (1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted alkanoyl,

(6) optionally substituted alkenoyl,

(7) optionally substituted alkynoyl,

(8) optionally substituted aroyl,

(9) optionally substituted aryl,

(10) optionally substituted cycloalkanoyl,

(11) optionally substituted cycloalkenoyl,

(12) optionally substituted alkylsulfonyl

(13) optionally substituted cycloalkyl

(14) optionally substituted cycloalkenyl

where the substituents on the alkyl, alkenyl, alkynyl, alkanoyl, alkenoyl, alkynoyl, aroyl, aryl, cycloalkanoyl, cycloalkenoyl, alkylsulfonyl, cycloalkyl and cycloalkenyl are from 1 to 10 groups independently selected from the group

consisting of hydroxy, alkoxy, cycloalkyl, aryl alkoxy, NR^gR^h, CO_2R_b, $CONR^cR^d$ and halogen,

(15) perfluoroalkyl,

(16) arylsulfonyl optionally substituted with 1 to 3 groups independently selected from alkyl, perfluoroalkyl, nitro, halogen and cyano,

(17) a 5- or 6-member heterocycle containing 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen optionally substituted by 1 to 4 groups independently selected from alkyl, alkenyl, perfluoroalkyl, amino, $C(O)NR^cR^d$, cyano, CO_2R^b and halogen, and which may be saturated or partly unsaturated;

R^b is (1) H,

(2) optionally substituted aryl,

(3) optionally substituted alkyl,

(4) optionally substituted alkenyl,

(5) optionally substituted alkynyl,

(6) optionally substituted cycloalkyl,

(7) optionally substituted cycloalkenyl, or

(8) optionally substituted heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen; where the substituents on the aryl, alkyl, alkenyl, cycloalkyl, cycloalkenyl, heterocycle, or alkynyl are from 1 to 10 groups

independently selected from

(i) hydroxy,

(ii) alkyl,

(iii) oxo,

(iv) $SO_2NR^gR^h$,

(v) arylalkoxy,

(vi) hydroxyalkyl,

(vii) alkoxy,

(viii) hydroxyalkoxy,

(ix) aminoalkoxy,

(x) cyano,

(xi) mercapto,

(xii) alkyl-$S(O)_m$,

(xiii) cycloalkyl optionally substituted

with 1 to 4 groups independently selected from R^e,

(xiv) cycloalkenyl,

(xv) halogen,

(xvi) alkanoyloxy,

(xvii) $C(O)NR^gR^h$,

(xviii) CO_2R^i,

(xix) formyl,

(xx) $-NR^gR^h$,

(xxi) 5 to 9-member heterocycle, which may be saturated or partially unsaturated, containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen, and optionally substituted with 1 to 5 groups independently selected from R^e,

(xxii) optionally substituted aryl, wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e,

(xxiii) optionally substituted arylalkoxy,

wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e, and

(xxiv) perfluoroalkyl;

R^c and R^d are independently selected from R^b; or

R^c and R^d together with the N to which they are attached form a 3- to 10-member ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^g, hydroxy, thioxo and oxo;

R^e is

(1) halogen,

(2) alkyl,

(3) perfluoroalkyl,

(4) $-S(O)_mR^i$,

(5) cyano,

(6) nitro,

(7) $R^iO(CH_2)_v$-,

(8) $R^iCO_2(CH_2)_v$-,

(9) $R^iOCO(CH_2)_v$-,

(10) optionally substituted aryl where the substituents are from 1 to 3 of halogen, alkyl, alkoxy, or hydroxy,

(11) $SO_2NR^gR^h$, or

(12) amino;

R^f is (1) alkyl,

(2) X-alkyl, where X is O or $S(O)_m$,

(3) alkenyl,

(4) alkynyl,

(5) perfluoroalkyl,

(6) NY^1Y^2, where Y^1 and Y^2 are independently H or alkyl,

(7) hydroxy,

(8) halogen, and

(9) alkanoyl amino,

R^g and R^h are independently

(1) hydrogen,

(2) alkyl optionally substituted with hydroxy, amino, or CO_2R^i

(3) aryl optionally substituted with halogen, 1,2-methylenedioxy, alkoxy, alkyl or perfluoroalkyl,

(4) arylalkyl, wherein the aryl is optionally substituted with perfluorolkyl or 1,2-methylenedioxy;

(5) alkoxycarbonyl,

(6) alkanoyl,

(7) alkanoylalkyl,

(9) arylalkoxycarbonyl,

(10) aminocarbonyl,

(11) monoalkylaminocarbonyl

(12) dialkylaminocarbonyl; or

mannitol, glycerol, sorbitol, polyoxyethylenated sorbitan esters; lecithin, sodium carboxymethylcellulose, and acrylic derivatives, or a mixture of these crystallization inhibitors.

3. The spot-on formulation according to claim 2 wherein

R_1 is (1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted cycloalkyl,

(6) optionally substituted cycloalkenyl where the substituents on the alkyl, alkenyl, alkynyl, cycloalkyl and cycloalkenyl are 1 to 3 groups independently selected from

(i) alkyl,

(ii) X-alkyl, where X is O or $S(O)_m$,

(iii) cycloalkyl,

(iv) hydroxy,

(v) halogen,

(vi) cyano,

(vii) carboxy, and

(viii) NY^1Y^2, where Y^1 and Y^2 are independently H or alkyl,

(7) aryl alkyl wherein said aryl is optionally substituted with 1 to 3 groups independently selected from R^f,

(8) perfluoroalkyl,

(9) a 5- or 6-member heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen atoms optionally substituted by 1 to 3 groups independently selected from hydroxy, oxo, alkyl and halogen, and which may be saturated or partly unsaturated,

R_8 is (1) H,

(2) OH, or

(3) NH_2;

R_9 is (1) H or

(2) OH;

R_{10} is (1) $C(O)OR^b$,

(2) $C(O)N(OR^b)R^c$,

(3) $C(O)NR^cR^d$,

(4) $NHC(O)OR^b$,

(5) $NHC(O)NR^cR^d$,

(6) CH_2OR^a,

(7) $CH_2OCO_2R^b$,

(8) $CH_2OC(O)NR^cR^d$,

(9) $C(O)NR^cNR^cR^d$, or

(10) $C(O)NR^cSO_2R^b$;

R^a is (1) hydrogen,

(2) optionally alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted alkanoyl,

(6) optionally substituted alkenoyl,

(7) optionally substituted alkynoyl,

(8) optionally substituted aroyl,

(9) optionally substituted aryl,

(10) optionally substituted cycloalkanoyl,

(11) optionally substituted cycloalkenoyl,

(12) optionally substituted alkylsulfonyl

(13) optionally substituted cycloalkyl

(14) optionally substituted cycloalkenyl where the substituents on the alkyl, alkenyl, alkynyl, alkanoyl, alkenoyl, alkynoyl, aroyl, aryl, cycloalkanoyl, cycloalkenoyl, alkylsulfonyl, cycloalkyl and cycloalkenyl are from 1 to 10 groups independently selected from hydroxy, alkoxy, cycloalkyl, aryl alkoxy, NR^gR^h, CO_2R^b, $CONR^cR^d$ and halogen,

(15) perfluoroalkyl,

(16) arylsulfonyl optionally substituted with 1 to 3 groups independently selected from alkyl, perfluoroalkyl, halogen and cyano,

(17) a 5- or 6-member heterocycle containing 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen optionally substituted by 1 to 4 groups independently selected from alkyl, alkenyl, perfluoroalkyl, amino, $C(O)NR^cR^d$, cyano, CO_2R^b and halogen, and which may be saturated or partly unsaturated;

R^b is (1) H,

(2) optionally substituted aryl,

(3) optionally substituted alkyl,

(4) optionally substituted alkenyl,

(5) optionally substituted alkynyl,

(6) optionally substituted cycloalkyl,

(7) optionally substituted cycloalkenyl, or

(8) optionally substituted 5- to 10-member heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen; where the substituents on the aryl, alkyl, alkenyl, cycloalkyl, cycloalkenyl, heterocycle, or alkynyl are from 1 to 10 groups independently selected from

(i) hydroxy,

(ii) alkyl,

(iii) oxo,

(iv) $SO_2NR^gR^h$,

(v) arylalkoxy,

(vi) hydroxyalkyl,

(vii) alkoxy,

(viii) hydroxyalkoxy,

(ix) aminoalkoxy,

(x) cyano,

(xi) perfluoroalkyl,

(xii) alkyl-$S(O)_m$,

(xiii) cycloalkyl optionally substituted

with 1 to 4 groups independently selected from R^e,

(xiv) cycloalkenyl,

(xv) halogen,

(xvi) alkanoyloxy,

(xvii) $C(O)NR^gR^h$,

(xviii) CO_2R^i,

(xix) optionally substituted aryl alkoxy,

wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e,

(xx) $-NR^gR^h$,

(xxi) 5 to 6-member heterocycle, which may be saturated or partially unsaturated, containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen, and optionally substituted with 1 to 5 groups independently selected from R^e, and

(xxii) optionally substituted aryl, wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from Re;

R^e is

(1) halogen,

(2) alkyl,

(3) perfluoroalkyl,

(4) $-S(O)_mR^i$,

(5) cyano,

(6) amino,

(7) $R^iO(CH_2)_v-$,

(8) $R^iCO_2(CH_2)_v-$,

(9) $R^iOCO(CH_2)_v-$,

(10) optionally substituted aryl where the substituents are from 1 to 3 of halogen, alkyl, alkoxy, or hydroxy, or

(11) $SO_2NR^gR^h$;

R^f is

(1) methyl,

(2) X-alkyl, where X is O or $S(O)_m$,

(3) halogen,

(4) acetylamino,

(5) trifluoromethyl,

(6) NY^1Y^2, where Y^1 and Y^2 are independently H or methyl, and

(7) hydroxy;

R^g and R^h are independently

(1) hydrogen,

(2) alkyl optionally substituted with hydroxy, amino, or CO_2R^i

(3) aryl optionally substituted with halogen, 1,2-methylenedioxy, alkoxy, alkyl or perfluoroalkyl,

(4) aryl alkyl, wherein the aryl is optionally substituted with perfluorolkyl or 1,2-methylenedioxy;

(5) alkoxycarbonyl,

(6) alkanoyl,

(7) alkanoylalkyl,

(9) arylalkoxycarbonyl,

(10) aminocarbonyl,

(11) monoalkylaminocarbonyl

(12) dialkylaminocarbonyl; or

R^g and R^h together with the N to which they are attached form a 5- to 6membered ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^e and oxo;

R^i is

(1) hydrogen,

(2) perfluoroalkyl,

(3) alkyl,

(4) optionally substituted aryl alkyl, where the aryl substituents are from 1 to 3 groups independently selected from halogen, alkyl, alkoxy, and hydroxy.

4. The spot-on formulation according to claim 2, wherein

R^1 is

(1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

where the substituents on the alkyl, alkenyl, and alkynyl are 1 to 3 groups independently selected from

(i) methyl,

(ii) X-methyl, where X is O or $S(O)_m$ and

(iii) halogen,

(5) arylalkyl wherein said aryl is optionally substituted with 1 to 3 groups independently selected from R^f.

(6) trifluoromethyl

R_8 is (1) H,

(2) OH, or

(3) NH_2

R_9 is (1) H, or

(2) OH;

R_{10} is (1) $C(O)OR^b$,

(2) $C(O)N(OR^b)R^c$,

(3) $C(O)NR^cR^d$,

(4) $NHC(O)OR^b$,

(5) $NHC(O)NR^cR^d$,

(6) CH_2OR^a,

(7) $CH_2OCO_2R^b$,

(8) $CH_2OC(O)NR^cR^d$,

(9) $C(O)NR^cNR^cR^d$, or

(10) $C(O)NR^cSO_2R^b$;

R^a is (1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted alkanoyl,

(6) optionally substituted aroyl,

(7) optionally substituted cycloalkanoyl,

(8) optionally substituted cycloalkenoyl,

(9) optionally substituted alkylsulfonyl

where the substituents on the alkyl, alkenyl, alkynyl, alkanoyl, aroyl, cycloalkanoyl, cycloalkenoyl, and alkylsulfonyl, are from 1 to 5 groups independently selected from hydroxy, alkoxy, aryl alkoxy, NR^gR^h, CO_2R^b, $CONR^cR^d$ and halogen,

(10) trifluoromethyl,

(11) arylsulfonyl optionally substituted with 1 to 3 groups independently selected from methyl, trifluoromethyl and halogen,

(12) a 5- or 6-member heterocycle containing 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen optionally substituted by 1 to 4 groups independently selected from methyl, trifluoromethyl, $C(O)NR^cR^d$, CO_2R^b and halogen, and which may be saturated or partly unsaturated;

R^b is (1) H,

(2) optionally substituted aryl,

(3) optionally substituted alkyl,

(4) optionally substituted alkenyl,

(5) optionally substituted alkynyl,

(6) optionally substituted cycloalkyl,

(7) optionally substituted cycloalkenyl, or

(8) optionally substituted 5- to 6-member heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen; where the substituents on the aryl, alkyl, alkenyl, cycloalkyl, cycloalkenyl, heterocycle, or alkynyl are from 1 to 10 groups independently selected from

(i) hydroxy,

(ii) alkyl,

(iii) oxo,

(iv) $SO_2NR^gR^h$,

(v) arylalkoxy,

(vi) hydroxyalkyl,

(vii) alkoxy,

(viii) hydroxyalkoxy,

(ix) aminoalkoxy,

(x) cyano,

(xi) alkyl-$S(O)_m$,

(xii) cycloalkyl optionally substituted with 1 to 4 groups independently selected from R^e,

(xiii) cycloalkenyl,

(xiv) halogen,

(xv) alkanoyloxy,

(xvi) $C(O)NR^gR^h$,

(xvii) CO_2R^i,

(xvii) $-NR^gR^h$,

(xix) 5 to 6-member heterocycle, which may be saturated or partially unsaturated, containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen, and optionally substituted with 1 to 5 groups independently selected from R^e,

(xx) optionally substituted aryl, wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e,

(xxi) optionally substituted aryl alkoxy, wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e, and

(xxii) perfluoroalkyl;

R^e is (1) halogen,

(2) alkyl,

(3) perfluoroalkyl,

(4) $-S(O)_mR^i$,

(5) cyano,

(6) $R^iO(CH_2)_v-$,

(7) $R^iCO_2(CH_2)_v-$,

(8) $R^iOCO(CH_2)_v-$,

R^g and R^h together with the N to which they are attached form a 3- to 7-member ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^e and oxo;

R^i is (1) hydrogen,

(2) perfluoroalkyl,

(3) alkyl,

(4) optionally substituted aryl, or arylalkyl, where the aryl substituents are from 1 to 3 groups independently selected from halogen, alkyl, alkoxy, and hydroxy;

m is 0 to 2; and

v is 0 to 3; or

a pharmaceutically acceptable salt thereof;

(2) a liquid carrier vehicle comprising a solvent and optionally a cosolvent wherein the solvent is selected from the group consisting of acetone, acetonitrile, benzyl alcohol, butyl diglycol, dimethylacetamide, dimethylformamide, dipropylene glycol n-butyl ether, ethanol, isopropanol, methanol, diethylene glycol monoethyl ether, ethylene glycol monomethyl ether, monomethylaceamide, dipropylene glycol monomethyl ether, liquid polyoxyethylene glycols, propylene glycol, 2-pyrrolidone, diethylene glycol monoethyl ether, ethylene glycol, diethyl phthalate, and a mixture of at least two of these solvents and the cosolvent is selected from the group consisting of absolute ethanol, isopropanol or methanol;

(3) optionally, a crystallization inhibitor selected from the group consisting of an anionic surfactant, a cationic surfactant, a non-ionic surfactant, an amine salt, an amphoteric surfactant, polyvinylpyrrolidone, polyvinyl alcohols, copolymers of vinyl acetate and vinylpyrrolidone, polyethylene glycols, benzyl alcohol,

(9) optionally substituted aryl where the substituents are from 1 to 3 of halogen, alkyl, alkoxy, or hydroxy,

(10) $SO_2NR^gR^h$, or

(11) amino;

R^f is (1) methyl,

(2) X-alkyl, where X is O or $S(O)_m$,

(3) trifluoromethyl,

(4) NY^1Y^2, where Y^1 and Y^2 are independently H or methyl,

(5) hydroxy,

(6) halogen, and

(7) acetylamino,

R^g and R^h are independently

(1) hydrogen,

(2) alkyl optionally substituted with hydroxy, amino, or CO_2R^i

(3) aryl optionally substituted with halogen, 1,2methylenedioxy, alkoxy, alkyl or perfluoroalkyl,

(4) aryl or arylalkyl, wherein the aryl is optionally substituted with perfluorolkyl or 1,2-methylenedioxy;

(5) alkoxycarbonyl,

(6) alkanoyl,

(7) alkanoylalkyl,

(9) arylalkoxycarbonyl,

(10) aminocarbonyl,

(11) monoalkylaminocarbonyl

(12) dialkylaminocarbonyl; or

R^g and R^h together with the N to which they are attached form a 5- to 6-member ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^e and oxo;

R^i is (1) hydrogen,

(2) perfluoroalkyl,

(3) alkyl,

(4) optionally substituted aryl or arylalkyl, where the aryl substituents are from 1 to 3 groups independently selected from halogen, alkyl, alkoxy, and hydroxy.

5. The spot-on formulation according to claim 2, wherein

R_{10} is $C(O)NR^cR^d$;

R^b is

(1) hydrogen,

(2) optionally substituted aryl,

(3) optionally substituted alkyl,

(4) optionally substituted alkenyl,

(5) optionally substituted alkynyl,

(6) optionally substituted cycloalkyl,

(7) optionally substituted cycloalkenyl, or

(8) optionally substituted 5 to 6-member heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen; where the substituents on the aryl, alkyl, alkenyl, cycloalkyl, cycloalkenyl, heterocycle, or alkynyl are from 1 to 10 groups independently selected from the group consisting of

(i) hydroxy,

(ii) alkyl,

(iii) oxo,

(iv) $SO_2NR^gR^h$,

(v) arylalkyl,

(vi) hydroxyalkylfoxy,

(viii) hydroxyalkoxy,

(ix) aminoalkoxy,

(x) cyano,

(xi) perfluoroalkyl,

(xii) alkyl-$S(O)_m$,

(xiii) cycloalkyl optionally substituted with 1 to 4 groups selected from R^e,

(xiv) cycloalkenyl,

(xv) halogen,

(xvi) $C(O)NR^gR^h$,

(xvii) CO_2R^i,

(xviii) $-NR^gR^h$,

(xix) 5 to 9-member heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen, and optionally substituted with 1 to 3 groups independently selected from R^e,

(xx) optionally substituted aryl, wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e and

(xxi) optionally substituted aryl alkoxy, wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e;

R^c and R^d are independently selected from R^b; or

R^c and R^d together with the N to which they are attached form a 3- to 10-member ring containing 0 to 2 additional heteratoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^g, hydroxy, thioxo and oxo;

R^e is

(1) halogen,

(2) alkyl,

(3) perfluoroalkyl,

(4) $R^iO(CH_2)v$-,

(5) $R^iCO_2(CH_2)v$-,

(6) $R^iOCO(CH_2)_v$-,

(7) $SO_2NR^gR^h$;

(8) amino

v is 0;

R^g and R^h are independently

(1) hydrogen,

(2) alkyl optionally substituted with hydroxy, amino, or CO_2R^i,

(3) aryl optionally substituted with halogen, 1,2-methylenedioxy, alkoxy, alkyl or perfluoroalkyl,

(4) aryl or arylalkyl, wherein the aryl is optionally substituted with perfluoroalkyl or 1,2methylenedioxy,

(5) alkoxycarbonyl,

(6) alkanoyl,

(7) arylalkoxycarbonyl,

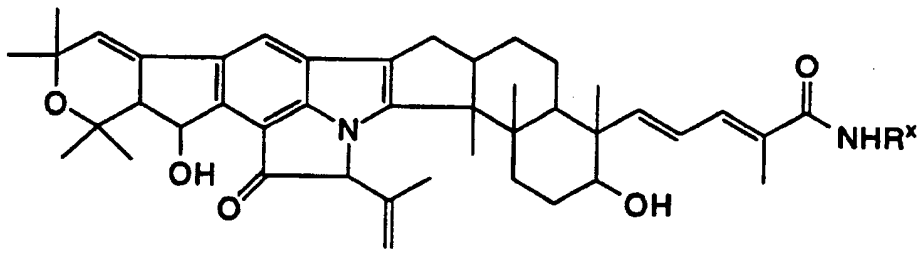
(8) aminocarbonyl, or

R^g and R^h together with the N to which they are attached form a 5- to 6-member ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^e and oxo;

R^i is (1) hydrogen or

(2) optionally substituted alkyl wherein the substituents are aryl or substituted aryl, and the aryl substituents are from 1 to 3 groups independently selected from halogen, alkyl, alkoxy, and hydroxy.

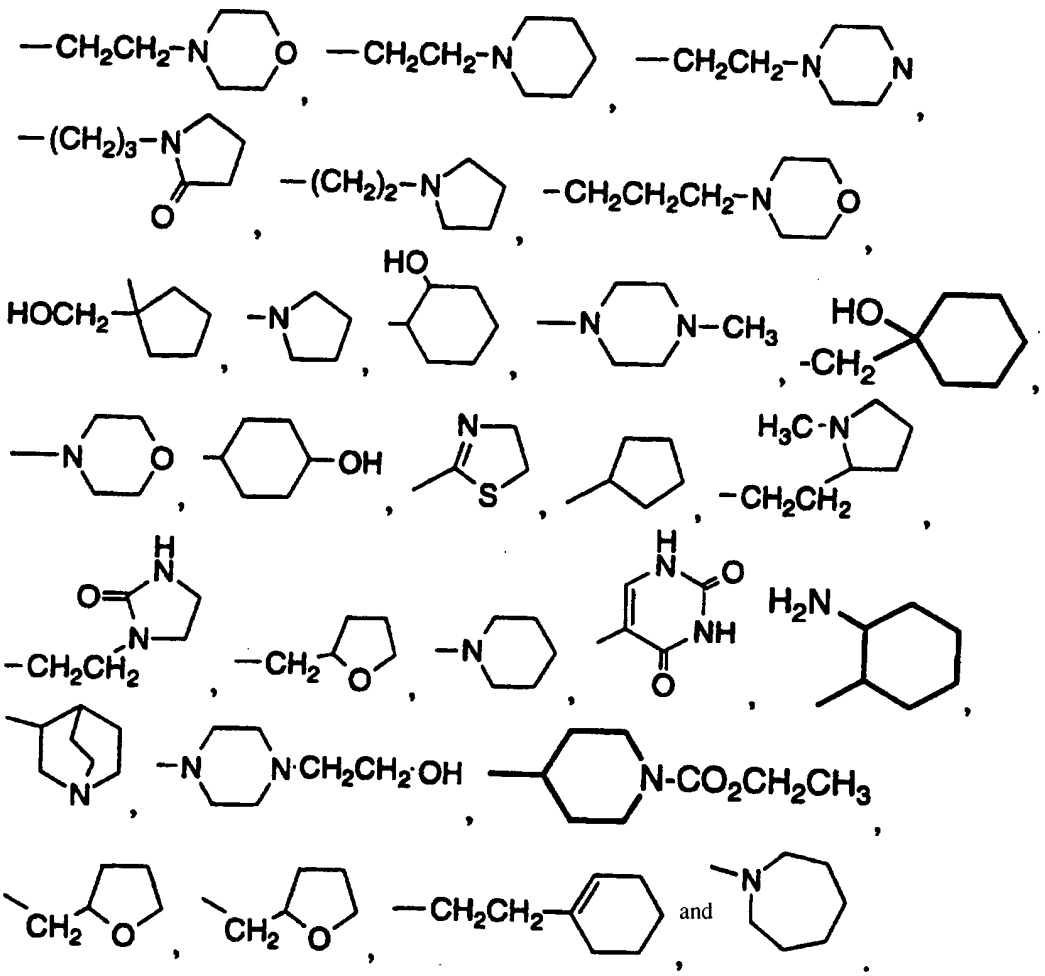
6. The spot-on formulation according to claim 2, wherein the nodulisporic acid derivative is a compound of the formula



wherein R^x is selected from the group consisting of:

H, CH_3, CH_2CH_3, $C(CH_3)_3$, $CH_2CH_2CH_3$, CH_2CH_2OH, $CH(CO_2CH_3)CH_2OH$, $CH_2CO_2CH_3$, $CH_2CH(OCH_2CH_3)_2$, $CH_2CH_2OCH_2CH_2OH$, $CH(CH_3)(CH_2)_3C(CH_3)_2OH$, $(CH_2)_3OH$, $(CH_2)_4OH$, $(CH_2)SOH$, $CH(CH_2OH)CH_2CH_3$, $NHC(CH_3)_3$, CH_2CN, $(CH_2)_6OH$, $CH_2CH(OH)CH_3$, $CH(CH_2OH)CH_2CH_2CH_3$, $CH_2CH_2SCH_3$, $CH_2CH_2SCH_2CH_3$, CH_2CONH_2,

$CH(CH_3)(CH_2OH)_2$, $CH_2CH_2NHCH_2CH_2OH$, $CH(CH_2OH)(CH_2)_3CH_3$, $CH(CH_2OCH_3)CH_3$, $(CH_2)_2SH$, $(CH_2)_4NH_2$, $CH_2CH_2SO_2CH_3$, $CH_2CH_2S(O)CH_3$, $CH(CH(CH_3)_2)CH_2OH$, $(CH_2)_3NH_2$, $(CH_2)_3N(CH_2CH_3)_2$, $(CH_2)_3N(CH_3)_2$, OCH_2CH_3, $CH_2CH(OH)CH_2OH$, OCH_3, $CH_2CH_2OCH_3$, $CH_2CH_2NHC(O)CH_3$, $C(CH_3)_2CH_2OH$, $c\text{-}C_3H_5$, cC_6H_{11}, $(CH_2)_3OCH_2CH_3$, $CH_2CH{=}CH_2$, $C(CH_2CH_3)(CH_2OH)_2$, $CH_2C{\equiv}CH$, $CH_2CO_2CH_2CH_3$, CH_2CH_2F, $(CH_2)_3O(CH_2)_{11}CH_3$, $CH_2CH_2N(CH_3)_2$, $CH_2CH_2OCH_2CH_2NH_2$, CH_2CF_3, $NHCH_2CO_2CH_2CH_3$, $CH(CH_3)CO_2CH_3$, $C(CH_3)_2CH_2C(O)CH_3$, $CH(CO_2CH_2CH_3)_2$, CH_2CH_3, $CH(CH_2CH_2CH_3)CO_2CH_3$, $CH_2CH_2CH_2OCH_3$, $C(CH_3)_2CH_2C{\equiv}CH$, $(CH_2)_4CH_3$, $CH(CH_2CH_2CH_3)_2$, $(CH_2)SCH_3$,$CH_2CH_2CO_2H$, $CH(CH(CH_3)_2)CO_2CH_3$, OCH_2CO_2H, $CH(CH(CH_3)_2)CH_2OH$, $CH(CH(CH_3)_2)CH_2OH$, $CH(CH_3)CH_2OH$, $CH(CH_3)CH_2OH$, $CH(CH_3)_2$, $(CH_2)CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2CH(CH_3)OH$, $(CH_2)_3CH_3$, $(CH_2)_2OCH_2CH_3$, 1-adamantyl, $(CH_2)_8CH_3$, $CH(CH_3)CH(CH_3)_2$, $(CH_2)_3NHCH_3$, $(CH_2)_2N(CH_2CH_3)_2$,



7. The spot-on formulation according to claim 6, wherein R^x is $C(CH_3)_3$.

8. The spot-on formulation according to claim 1, wherein the liquid carrier vehicle comprises a microemulsion.

9. The spot-on formulation according to claim 6, wherein the liquid carrier vehicle further comprises an excipient.

10. The spot-on formulation according to claim 9, wherein the excipient is C_8-C_{10} caprylic/capric triglycerides, oleic acid or propylene glycol.

11. The spot-on formulation according to claim 10, wherein the spot-on formulation further comprises an antioxidant.

12. The spot-on formulation according to claim 11, wherein the antioxidant is selected from the group consisting of butylated hydroxyanisole, butylated hydroxytoluene, ascorbic acid, sodium metabisulphite, propyl gallate, and sodium thiosulphate.

13. The spot-on formulation according to claim 12, wherein the compound of formula (I) is t-butyl nodulisporamide, the carrier medium comprises diethylene glycol monoethyl ether and C_8-C_{10} caprylic/capric triglycerides, and the antioxidant is butylated hydroxytoluene.

14. The spot-on formulation according to claim 2, wherein the combination comprises about 0.001 to about 100 mg/kg of weight of mammal or bird of a compound of formula (I).

15. The spot-on formulation according to claim 7, wherein the combination comprises about 1 to about 50 mg/kg of weight of mammal or bird of a compound of formula (I).

16. The spot-on formulation according to claim 2, which comprises crystallization inhibitor and further comprises an antioxidant.

17. The spot-on formulation wherein the compound of formula (I) is t-butyl nodulisporamide.

18. The spot-on formulation according to claim 16, wherein about 0.005 to about 1% (W/V) of antioxidant is present and the antioxidant is selected from the group consisting of butylated hydroxyanisole, butylated hydroxytoluene, ascorbic acid, sodium metabisulphite, propyl gallate, and sodium thiosulphate.

19. The spot-on formulation according to claim 18, wherein the crystallization inhibitor is present in an amount from about 1 to about 20% W/V.

20. The spot-on formulation according to claim 19, wherein

- the anionic surfactant is alkaline stearates, sodium abietate; alkyl sulphates; sodium dodecylbenzenesulphonate, sodium dioctylsulphosuccinate; and fatty acids;
- the cationic surfactant is water-soluble quaternary ammonium salts of formula $N^+RR"R'"R"" Y^-$ in which the radicals R independently are hydrocarbon radicals, optionally hydroxylated, and Y^- is an anion of a strong acid;
- the amine salt is an amine salt of $N^+RR"R'"$ in which the radicals R independently are optionally hydroxylated hydrocarbon radicals;
- the non-ionic surfactant is optionally polyoxyethylenated sorbitan esters, polyoxyethylenated alkyl ethers; polyethylene glycol stearate, polyoxyethylenated derivatives of castor oil, polyglycerol esters, polyoxyethylenated fatty alcohols, polyoxyethylenated fatty acids, copolymers of ethylene oxide and propylene oxide; and
- the amphoteric surfactant is lauryl-substituted betaine compounds.

21. The spot-on formulation according to claim 19, where the crystallization inhibitor is a crystallization inhibitor system comprising a polymeric film-forming agent and a surfactant.

22. The spot-on formulation according to claim 21, wherein the polymeric film-forming agent is polyvinylpyrrolidone, polyvinyl alcohols, or a copolymer of vinyl acetate and polyvinylpyrrolidone and the surfactant is a non-ionic surfactant.

23. The spot-on formulation according to claim 22, wherein the crystallization inhibitor system is a mixture of polyvinylpyrrolidone and polyoxethylene (20) sorbitan mono-oleate.

24. The spot-on formulation according to claim 18, wherein the compound of formula (I) is t-butyl nodulisporamide, the liquid carrier vehicle is diethylene glycol monoethyl ether, the crystallization inhibitor is pyrrolidone and the antioxidant is butylated hydroxytoluene.

25. A method of treating parasite infestations or for the prophylaxis of parasite infestation in mammals, fish or birds which comprises applying to said mammals, fish or birds an effective amount of a spot-on composition according to claim 1.

26. The method according to claim 25, wherein the parasite is an ectoparasite.

27. The method according to claim 25, wherein the parasite is an endoparasite.

28. The method according to claim 25, wherein the mammal is a cat, dog, horse, cattle or sheep.

29. The method according to claim 28, wherein the parasite is a flea or tick.

30. The method according to claim 25, wherein the mammal is a human.

31. The method according to claim 25, wherein the ectoparasites are mites, ticks, mosquitoes, flies or a combination of the foregoing.

32. A method of treating parasite infestations or for the prophylaxis of parasite infestations in mammals or birds which comprises applying to said mammals or birds an effective amount of a spot-on formulation according to claim 13.

33. The method according to claim 32 wherein the parasite is a flea or tick and the mammal is a cat or dog.

34. The method of claim 25, wherein the administration is bimonthly.

35. The method of claim 25, wherein the administration is quarterly.

36. The method of claim 25, wherein the administration is monthly.

37. A method for treating parasite infestations or for the prophylaxis of parasite infestations in mammals or birds which comprises applying to said mammal or bird an effective amount of a spot-on formulation according to claim 24.

38. The method according to claim 37 wherein the mammal is a cat or dog and the parasite is a flea or tick.

39. The method of claim 37, wherein the administration is bimonthly.

40. The method of claim 37, wherein the administration is quarterly.

41. The method of claim 37, wherein the administration is monthly.

42. A spot-on formulation for combating parasites in a mammal which comprises applying a composition according to claim 6 for a localized cutaneous application to said mammal with absorption and a resultant plasma concentration of the compound(s) of formula (I) wherein the liquid carrier vehicle comprises diethylene glycol monoethyl ether, and at least one antioxidant.

43. The spot-on formulation according to claim 42 which further comprises a crystallization inhibitor.

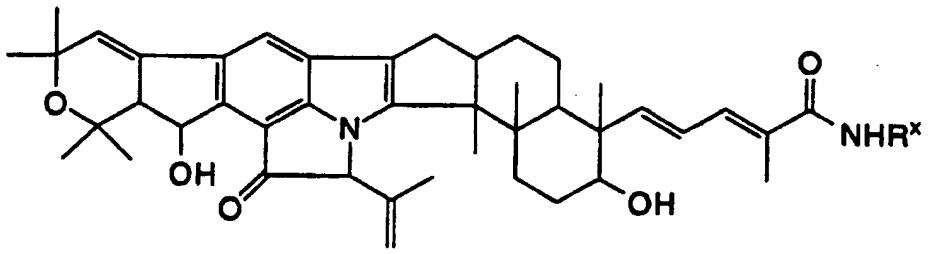
44. The spot-on formulation as claimed in claim 43, wherein an antioxidant is BHT and the crystallization inhibitor is pyrrolidone.

45. A method for combating parasites in a mammal comprising topically administering to a mammal a parasiticically effective amount of a spot-on formulation according to claim 42.

46. The method according to claim 45, wherein the mammal is a cat or dog and the parasite is a flea or tick.

47. A method for obtaining a detectable plasma concentration of parasiticides in a mammal comprising topically applying to a localized area on said mammal a parasiticically effective amount of the spot-on formulation as claimed in claim 42.

48. A method for combating parasites of a cat or dog comprising localized cutaneous application to the cat or dog, between the shoulders, at a frequency not greater than monthly, of a spot-on composition, which comprises, in a veterinarily acceptable vehicle, an effect amount parasitically effective amount of at least one of the formula



wherein R^x is selected from the group consisting of:

H, CH_3, CH_2CH_3, $C(CH_3)_3$, $CH_2CH_2CH_3$, CH_2CH_2OH, $CH(CO_2CH_3)CH_2OH$, $CH_2CO_2CH_3$, $CH_2CH(OCH_2CH_3)_2$, $CH_2CH_2OCH_2CH_2OH$, $CH(CH_3)(CH_2)_3C(CH_3)_2OH$, $(CH_2)_3OH$, $(CH_2)_4OH$, $(CH_2)SOH$, $CH(CH_2OH)CH_2CH_3$, $NHC(CH_3)_3$, CH_2CN, $(CH_2)_6OH$, $CH_2CH(OH)CH_3$, $CH(CH_2OH)CH_2CH_2CH_3$, $CH_2CH_2SCH_3$, $CH_2CH_2SCH_2CH_3$, CH_2CONH_2, $CH(CH_3)(CH_2OH)_2$, $CH_2CH_2NHCH_2CH_2OH$, $CH(CH_2OH)(CH_2)_3CH_3$, $CH(CH_2OCH_3)CH_3$, $(CH_2)_2SH$, $(CH_2)_4NH_2$, $CH_2CH_2SO_2CH_3$, $CH_2CH_2S(O)CH_3$, $CH(CH(CH_3)_2)CH_2OH$, $(CH_2)_3NH_2$, $(CH_2)_3N(CH_2CH_3)_2$, $(CH_2)_3N(CH_3)_2$, OCH_2CH_3, $CH_2CH(OH)CH_2OH$, OCH_3, $CH_2CH_2OCH_3$, $CH_2CH_2NHC(O)CH_3$, $C(CH_3)_2CH_2OH$, c-C_3H_5, cC_6H_{11}, $(CH_2)_3OCH_2CH_3$, $CH_2CH{=}CH_2$,

$C(CH_2CH_3)(CH_2OH)_2$, $CH_2C{\equiv}CH$, $CH_2CO_2CH_2CH_3$, CH_2CH_2F, $(CH_2)_3O(CH_2)_{11}CH_3$, $CH_2CH_2N(CH_3)_2$, $CH_2CH_2OCH_2CH_2NH_2$, CH_2CF_3, $NHCH_2CO_2CH_2CH_3$, $CH(CH_3)CO_2CH_3$, $C(CH_3)_2CH_2C(O)CH_3$, $CH(CO_2CH_2CH_3)_2$, CH_2CH_3, $CH(CH_2CH_2CH_3)CO_2CH_3$, $CH_2CH_2CH_2OCH_3$, $C(CH_3)_2CH_2C{\equiv}CH$, $(CH_2)_4CH_3$, $CH(CH_2CH_2CH_3)_2$, $(CH_2)SCH_3$,$CH_2CH_2CO_2H$, $CH(CH(CH_3)_2)CO_2CH_3$, OCH_2CO_2H, $CH(CH(CH_3)_2)CH_2OH$, $CH(CH(CH_3)_2)CH_2OH$, $CH(CH_3)CH_2OH$, $CH(CH_3)CH_2OH$, $CH(CH_3)_2$, $(CH_2)CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2CH(CH_3)OH$, $(CH_2)_3CH_3$, $(CH_2)_2OCH_2CH_3$, 1-adamantyl, $(CH_2)_8CH_3$, $CH(CH_3)CH(CH_3)_2$, $(CH_2)_3NHCH_3$, $(CH_2)_2N(CH_2CH_3)_2$,

the vehicle is for a localized cutaneous application to the animal between the shoulders and contains an organic solvent, an antioxidant and/or a crystallization inhibitor wherein:

the organic solvent comprises acetone, ethyl acetate, methanol, ethanol, isopropanol, dimethylformamide, dichloromethane or diethyl glycol monoethyl ether; said solvent optionally supplemented by C_8-C_{10} caprylic/capric triglyceride, oleic acid or propylene glycol;

the antioxidant is selected from the group consisting of butylated hydroxyanisole, butylated hydroxytoluene, ascorbic acid, sodium metabisuphite, propylgallate, and sodium theosulphate; and

the crystallization inhibitor selected from the group consisting of polyvinylpyrrolidone, copolymers of vinyl acetate and vinylpyrrolidone, polyoxyethylenated sorbitan esters and mixtures thereof;

whereby there is a prolonged release of formula (I) in or on the body of the cat or dog.

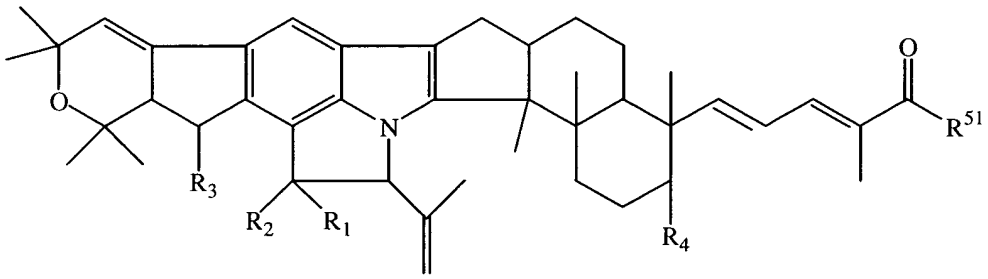
49. The method of claim 48 wherein in the spot-on composition the compound of formula (I) is t-butyl nodulisporamide.

50. The method of claim 48 wherein compound of formula (I) is present in the spot-on composition in an amount of from about 0.1 to about 100 mg/kg of weight of animal.

51. The method according to claim 49 wherein the liquid carrier vehicle is diethylene glycol monoethyl ether and the antioxidant is butylated hydroxytoluene.

52. The method of claim 49 wherein the spot-on composition comprises an antioxidant and the antioxidant is polyvinylpyrrolidone.

53. A process for the preparation of a compound having the formula:



I'

wherein

R_1 is (1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted cycloalkyl,

(6) optionally substituted cycloalkenyl,

where the substituents on the alkyl, alkenyl, alkynyl,

cycloalkyl and cycloalkenyl are 1 to 3 groups independently selected from

(i) alkyl,

(ii) X-alkyl, where X is O or $S(O)_m$,

(iii) cycloalkyl,

(iv) hydroxy,

(v) halogen,

(vi) cyano,

(vii) carboxy,

(viii) NY^1Y^2, where Y^1 and Y^2 are independently H or alkyl,

(ix) alkanoylamino, and

(x) aroylamino wherein said aroyl is optionally substituted with 1 to 3 groups independently selected from R^f

(7) aryl or arylalkyl wherein said aryl is optionally substituted with 1 to 3 groups independently selected from R^f,

(8) perfluoroalkyl

(9) a 5- or 6-member heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen atoms optionally substituted by 1 to 3 groups independently selected from hydroxy, oxo, alkyl and halogen, and which may be saturated or partly unsaturated,

R_2, R_3, and R_4 are independently OR^a, OCO_2R^b, $OC(O)NR^cR^d$; or

R_1 and R_2 represent =O, $=NOR^a$ or $=N\text{-}NR^cR^d$;

R^a is

(1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted alkanoyl,

(6) optionally substituted alkenoyl,

(7) optionally substituted alkynoyl,

(8) optionally substituted aroyl,

(9) optionally substituted aryl,

(10) optionally substituted cycloalkanoyl,

(11) optionally substituted cycloalkenoyl,

(12) optionally substituted alkylsulfonyl

(13) optionally substituted cycloalkyl

(14) optionally substituted cycloalkenyl

where the substituents on the alkyl, alkenyl, alkynyl, alkanoyl, alkenoyl, alkynoyl, aroyl, aryl, cycloalkanoyl, cycloalkenoyl, alkylsulfonyl, cycloalkyl and cycloalkenyl are from 1 to 10 groups independently selected from the group consisting of hydroxy, alkoxy, cycloalkyl, aryl alkoxy, NR^gR^h, CO_2R_b, $CONR^cR^d$ and halogen,

(15) perfluoroalkyl,

(16) arylsulfonyl optionally substituted with 1 to 3 groups independently selected from alkyl, perfluoroalkyl, nitro, halogen and cyano,

(17) a 5- or 6-member heterocycle containing 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen optionally substituted by 1 to 4 groups independently selected from alkyl, alkenyl, perfluoroalkyl, amino, $C(O)NR^cR^d$, cyano, CO_2R^b and halogen, and which may be saturated or partly unsaturated;

R^b is (1) H,

(2) optionally substituted aryl,

(3) optionally substituted alkyl,

(4) optionally substituted alkenyl,

(5) optionally substituted alkynyl,

(6) optionally substituted cycloalkyl,

(7) optionally substituted cycloalkenyl, or

(8) optionally substituted heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen; where the substituents on the aryl, alkyl, alkenyl, cycloalkyl, cycloalkenyl, heterocycle, or alkynyl are from 1 to 10 groups

independently selected from

(i) hydroxy,

(ii) alkyl,

(iii) oxo,

(iv) $SO_2NR^gR^h$,

(v) arylalkoxy,

(vi) hydroxyalkyl,

(vii) alkoxy,

(viii) hydroxyalkoxy,

(ix) aminoalkoxy,

(x) cyano,

(xi) mercapto,

(xii) alkyl-$S(O)_m$,

(xiii) cycloalkyl optionally substituted

with 1 to 4 groups independently selected from R^e,

(xiv) cycloalkenyl,

(xv) halogen,

(xvi) alkanoyloxy,

(xvii) $C(O)NR^gR^h$,

(xviii) CO_2R^i,

(xix) formyl,

(xx) $-NR^gR^h$,

(xxi) 5 to 9-member heterocycle, which may be saturated or partially unsaturated, containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen, and optionally substituted with 1 to 5 groups independently selected from R^e,

(xxii) optionally substituted aryl, wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e,

(xxiii) optionally substituted arylalkoxy,

wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e, and

(xxiv) perfluoroalkyl;

R^c and R^d are independently selected from R^b; or

R^c and R^d together with the N to which they are attached form a 3- to 10-member ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^g, hydroxy, thioxo and oxo;

R^e is

(1) halogen,

(2) alkyl,

(3) perfluoroalkyl,

(4) $-S(O)_mR^i$,

(5) cyano,

(6) nitro,

(7) $R^iO(CH_2)_v-$,

(8) $R^iCO_2(CH_2)_v-$,

(9) $R^iOCO(CH_2)_v-$,

(10) optionally substituted aryl where the substituents are from 1 to 3 of halogen, alkyl, alkoxy, or hydroxy,

(11) $SO_2NR^gR^h$, or

(12) amino;

R^f is

(1) alkyl,

(2) X-alkyl, where X is O or $S(O)_m$,

(3) alkenyl,

(4) alkynyl,

(5) perfluoroalkyl,

(6) NY^1Y^2, where Y^1 and Y^2 are independently H or alkyl,

(7) hydroxy,

(8) halogen, and

(9) alkanoyl amino,

R^g and R^h are independently

(1) hydrogen,

(2) alkyl optionally substituted with hydroxy, amino, or CO_2R^i

(3) aryl optionally substituted with halogen, 1,2-methylenedioxy, alkoxy, alkyl or perfluoroalkyl,

(4) arylalkyl, wherein the aryl is optionally substituted with perfluorolkyl or 1,2-methylenedioxy;

(5) alkoxycarbonyl,

(6) alkanoyl,

(7) alkanoylalkyl,

(9) arylalkoxycarbonyl,

(10) aminocarbonyl,

(11) monoalkylaminocarbonyl

(12) dialkylaminocarbonyl; or

R^g and R^h together with the N to which they are attached form a 3- to 7-member ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^e and oxo;

R^i is (1) hydrogen,

(2) perfluoroalkyl,

(3) alkyl,

(4) optionally substituted aryl, or arylalkyl, where the aryl substituents are from 1 to 3 groups independently selected from halogen, alkyl, alkoxy, and hydroxy;

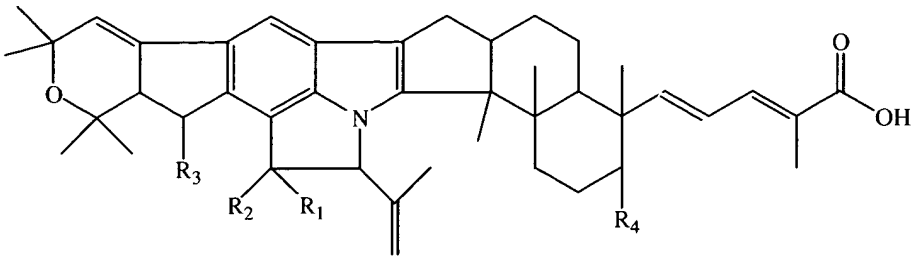
m is 0 to 2; and

v is 0 to 3;

R^{51} is R^c and R^d

or a pharmaceutically acceptable salt thereof which comprises

(1) coupling a compound of formula II':

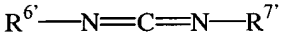


II'

wherein

R_1, R_2, R_3, and R_4 are defined above,

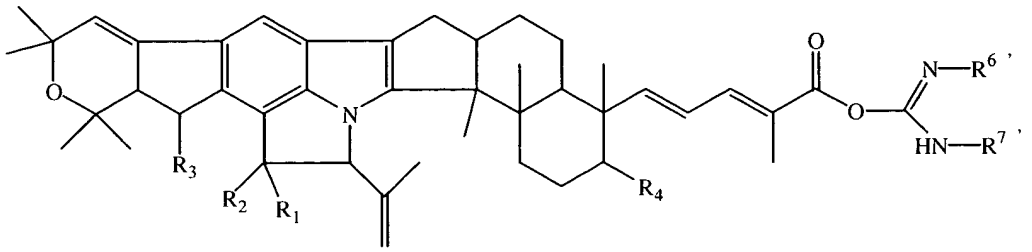
with a compound of formula III:



III

wherein $R^{6'}$ and $R^{7'}$ can be independently selected from alkyl and cycloalkyl,

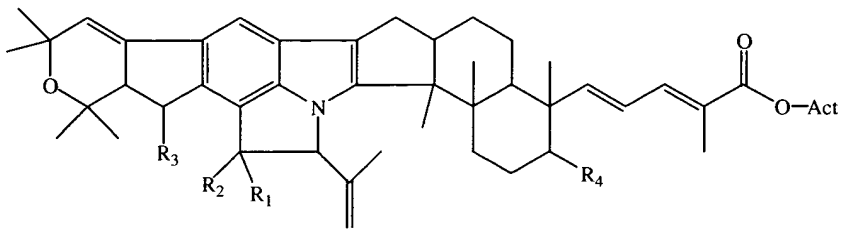
in the presence of an organic solvent to produce a first intermediate compound, of the formula



V'

(2) reacting the first intermediate compound with an activating compound, Act

to produce a second intermediate compound of the formula:

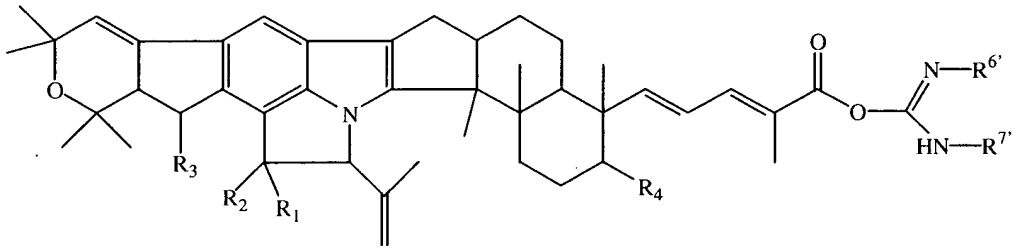


VI'

(3) adding an alkyl amine of the formula HNR^cR^d to the second intermediate compound to obtain a compound of formula I'.

54. The process according to claim 53, wherein the activating compound is 1-hydroxybenzotriazole, 2-hydroxypyridine-N-oxide, 2-hydroxypyridine and hydroxysuccinimide.

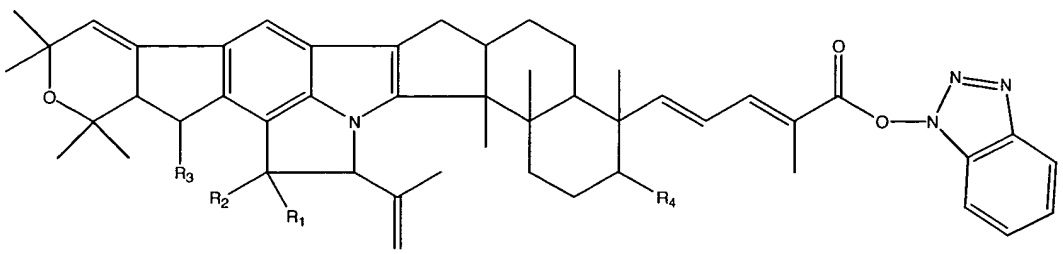
55. The process according to claim 53 wherein the first intermediate compound has the formula



V'

wherein $R^{6'}$ and $R^{7'}$ can be independently selected from alkyl and cycloalkyl, or a pharmaceutically acceptable salt thereof.

56. The process according to claim 53 wherein the second intermediate compound has the formula



VI'

or a pharmaceutically acceptable salt thereof.

57. The process according to claim 53 wherein said organic solvent is a halogenated hydrocarbon or a mixture of halogenated hydrocarbons.

58. The process according to claim 53 wherein said organic solvent is an ether or a mixture of ethers.

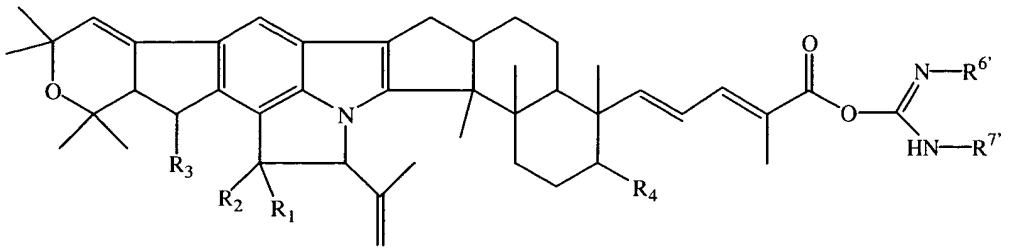
59. The process according to claim 56 wherein said halogenated hydrocarbon is methlyene chloride.

60. The process according to claim 57 wherein said ether or mixture of ethers are selected from the group consisting of tetrahydrofuran, diethyl ether, and methyl t-butyl ether.

61. The process according to claim 52 wherein the process is which is carried out in a single step without the isolation of a first and second intermediate compounds.

62. The process according to claim 53 which is carried out step-wise with the isolation of a first and/or second intermediate compounds.

63. A compound of the formula:



V'

wherein

R_1 is (1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted cycloalkyl,

(6) optionally substituted cycloalkenyl,

where the substituents on the alkyl, alkenyl, alkynyl, cycloalkyl and cycloalkenyl are 1 to 3 groups independently selected from

(i) alkyl,

(ii) X-alkyl, where X is O or $S(O)_m$,

(iii) cycloalkyl,

(iv) hydroxy,

(v) halogen,

(vi) cyano,

(vii) carboxy,

(viii) NY^1Y^2, where Y^1 and Y^2 are independently H or alkyl,

(ix) alkanoylamino, and

(x) aroylamino wherein said aroyl is optionally substituted with 1 to 3 groups independently selected from R^f

(7) aryl or arylalkyl wherein said aryl is optionally substituted with 1 to 3 groups independently selected from R^f,

(8) perfluoroalkyl

(9) a 5- or 6-member heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen atoms optionally substituted by 1 to 3 groups independently selected from hydroxy, oxo, alkyl and halogen, and which may be saturated or partly unsaturated,

R_2, R_3, and R_4 are independently OR^a, OCO_2R^b, $OC(O)NR^cR^d$; or

R_1 and R_2 represent =O, $=NOR^a$ or $=N\text{-}NR^cR^d$;

R^a is

(1) hydrogen,

(2) optionally substituted alkyl,

(3) optionally substituted alkenyl,

(4) optionally substituted alkynyl,

(5) optionally substituted alkanoyl,

(6) optionally substituted alkenoyl,

(7) optionally substituted alkynoyl,

(8) optionally substituted aroyl,

(9) optionally substituted aryl,

(10) optionally substituted cycloalkanoyl,

(11) optionally substituted cycloalkenoyl,

(12) optionally substituted alkylsulfonyl

(13) optionally substituted cycloalkyl

(14) optionally substituted cycloalkenyl

where the substituents on the alkyl, alkenyl, alkynyl, alkanoyl, alkenoyl, alkynoyl, aroyl, aryl, cycloalkanoyl, cycloalkenoyl, alkylsulfonyl, cycloalkyl and cycloalkenyl are from 1 to 10 groups independently selected from the group consisting of hydroxy, alkoxy, cycloalkyl, aryl alkoxy, NR^gR^h, CO_2R_b, $CONR^cR^d$ and halogen,

(15) perfluoroalkyl,

(16) arylsulfonyl optionally substituted with 1 to 3 groups independently selected from alkyl, perfluoroalkyl, nitro, halogen and cyano,

(17) a 5- or 6-member heterocycle containing 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen optionally substituted by 1 to 4 groups independently selected from alkyl, alkenyl, perfluoroalkyl, amino, $C(O)NR^cR^d$, cyano, CO_2R^b and halogen, and which may be saturated or partly unsaturated;

R^b is (1) H,

(2) optionally substituted aryl,

(3) optionally substituted alkyl,

(4) optionally substituted alkenyl,

(5) optionally substituted alkynyl,

(6) optionally substituted cycloalkyl,

(7) optionally substituted cycloalkenyl, or

(8) optionally substituted heterocycle containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen; where the substituents on the aryl, alkyl, alkenyl, cycloalkyl, cycloalkenyl, heterocycle, or alkynyl are from 1 to 10 groups

independently selected from

(i) hydroxy,

(ii) alkyl,

(iii) oxo,

(iv) $SO_2NR^gR^h$,

(v) arylalkoxy,

(vi) hydroxyalkyl,

(vii) alkoxy,

(viii) hydroxyalkoxy,

(ix) aminoalkoxy,

(x) cyano,

(xi) mercapto,

(xii) alkyl-$S(O)_m$,

(xiii) cycloalkyl optionally substituted

with 1 to 4 groups independently selected from R^e,

(xiv) cycloalkenyl,

(xv) halogen,

(xvi) alkanoyloxy,

(xvii) $C(O)NR^gR^h$,

(xviii) CO_2R^i,

(xix) formyl,

(xx) $-NR^gR^h$,

(xxi) 5 to 9-member heterocycle, which may be saturated or partially unsaturated, containing from 1 to 4 heteroatoms independently selected from oxygen, sulfur and nitrogen, and optionally substituted with 1 to 5 groups independently selected from R^e,

(xxii) optionally substituted aryl, wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e,

(xxiii) optionally substituted arylalkoxy,

wherein the aryl substituents are 1,2-methylenedioxy or 1 to 5 groups independently selected from R^e, and

(xxiv) perfluoroalkyl;

R^c and R^d are independently selected from R^b; or

R^c and R^d together with the N to which they are attached form a 3- to 10-member ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^g, hydroxy, thioxo and oxo;

R^e is

(1) halogen,

(2) alkyl,

(3) perfluoroalkyl,

(4) $-S(O)_mR^i$,

(5) cyano,

(6) nitro,

(7) $R^iO(CH_2)_v-$,

(8) $R^iCO_2(CH_2)_v-$,

(9) $R^iOCO(CH_2)_v$-,

(10) optionally substituted aryl where the substituents are from 1 to 3 of halogen, alkyl, alkoxy, or hydroxy,

(11) $SO_2NR^gR^h$, or

(12) amino;

R^f is (1) alkyl,

(2) X-alkyl, where X is O or $S(O)_m$,

(3) alkenyl,

(4) alkynyl,

(5) perfluoroalkyl,

(6) NY^1Y^2, where Y^1 and Y^2 are independently H or alkyl,

(7) hydroxy,

(8) halogen, and

(9) alkanoyl amino,

R^g and R^h are independently

(1) hydrogen,

(2) alkyl optionally substituted with hydroxy, amino, or CO_2R^i

(3) aryl optionally substituted with halogen, 1,2-methylenedioxy, alkoxy, alkyl or perfluoroalkyl,

(4) arylalkyl, wherein the aryl is optionally substituted with perfluorolkyl or 1,2-methylenedioxy;

(5) alkoxycarbonyl,

(6) alkanoyl,

(7) alkanoylalkyl,

(9) arylalkoxycarbonyl,

(10) aminocarbonyl,

(11) monoalkylaminocarbonyl

(12) dialkylaminocarbonyl; or

R^g and R^h together with the N to which they are attached form a 3- to 7-member ring containing 0 to 2 additional heteroatoms selected from O, $S(O)_m$, and N, optionally substituted with 1 to 3 groups independently selected from R^e and oxo;

R^i is (1) hydrogen,

(2) perfluoroalkyl,

(3) alkyl,

(4) optionally substituted aryl, or arylalkyl, where the aryl substituents are from 1 to 3 groups independently selected from halogen, alkyl, alkoxy, and hydroxy;

m is 0 to 2; and

v is 0 to 3;

$R^{6'}$ and $R^{7'}$ can be independently selected from alkyl and cycloalkyl, or a salt thereof.